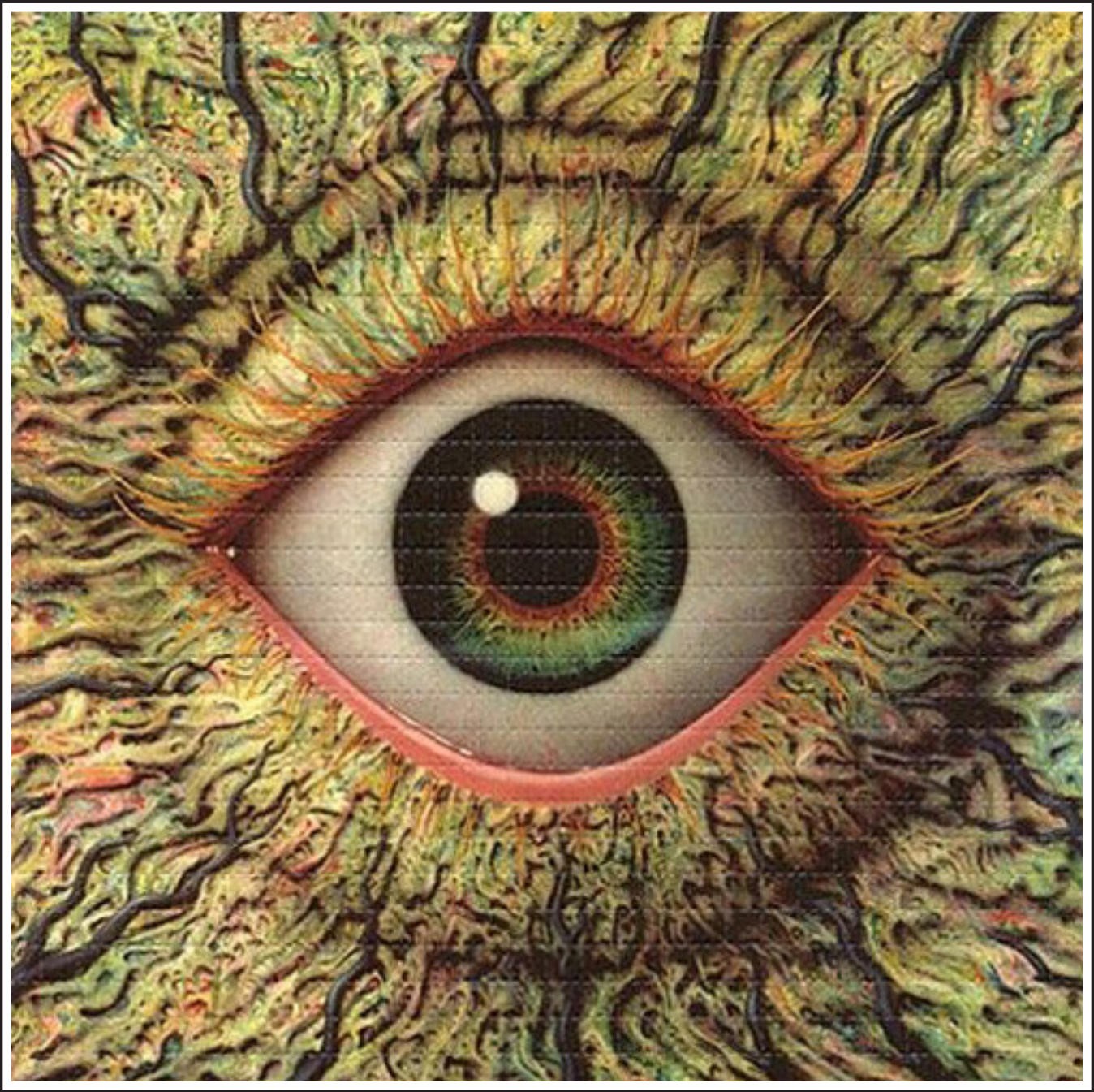
LSD

The History, The Narrative & The Peer Review
By The People That Were There



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"It opened my eyes. It would mean a whole new world if the politicians would take LSD. There wouldn't be any more war or poverty or famine"

~ Sir Paul McCartney

"SPLENDOR IN THE GRASS" or "CAUGHT NAPPING"

R.CRUMB '96

10 1/2 (OR 12) x 10 3/8

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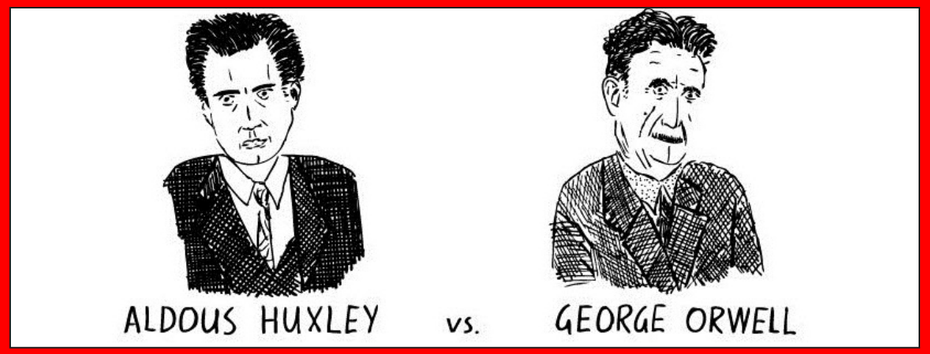
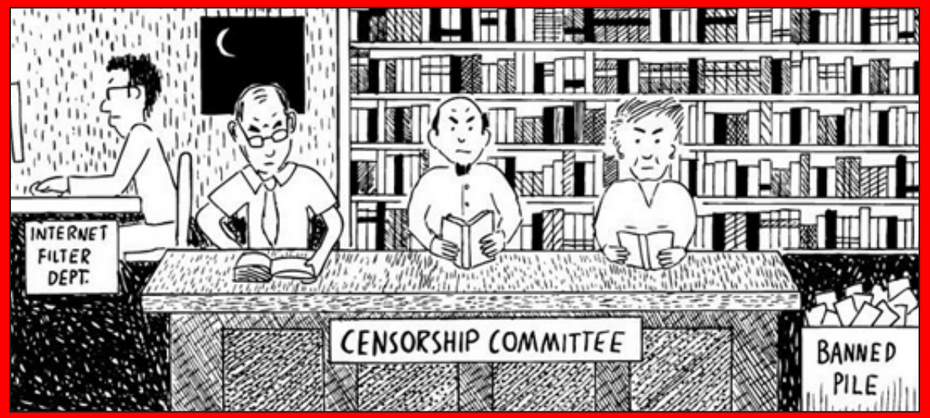
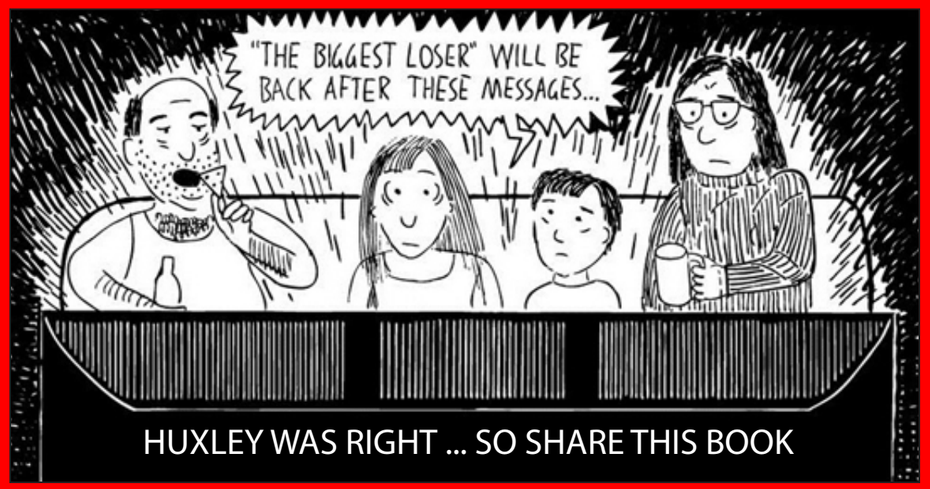


What ORWELL FEARED WERE THOSE WHO WOULD BAN BOOKS

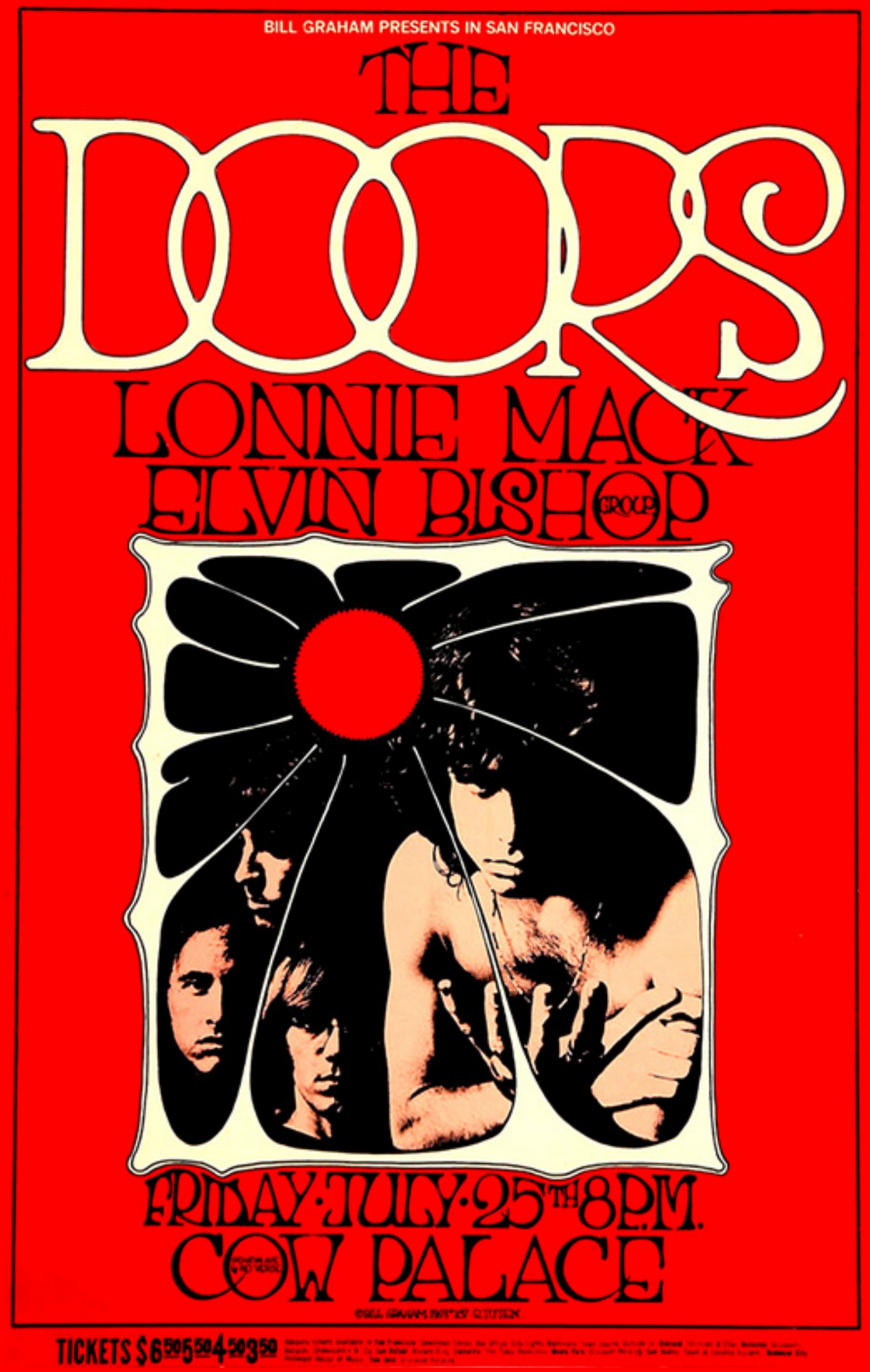


What huxley FEARED Was that there would be no reason to BAN BOOKS because there would be no one that would want to read them



screening. When administered under supportive conditions, psilocybin occasioned experiences similar to spontaneously occurring mystical experiences that, at 14-month follow-up, were considered by volunteers to be among the most personally meaningful and spiritually significant of their lives.

Classic hallucinogens (e.g. psilocybin and LSD) have substantial effects on perception, cognition, and emotion that can often be psychologically challenging, however we know very little regarding the source of significant individual variability that has been observed in the frequency and intensity of challenging experiences (i.e. "bad trips") with psychedelics. Previous clinical and observational literature suggests that there may be an association between neuroticism and challenging psychedelic experiences. Data from two online surveys of challenging experiences with psilocybin were analyzed. Multivariate analysis was used to estimate the associations between total score and scores from seven sub-factors (fear, grief, physical distress, insanity, isolation, death, and paranoia) of the Challenging Experience Questionnaire (CEQ), and scale scores from the Ten Item Personality Inventory (TIPI) in Study 1 (N=1993) and the Big Five Inventory (BFI) in Study 2 (N = 981). CEQ scores were negatively associated with emotional stability scores (the inverse of neuroticism) in Study 1 and positively associated with neuroticism scores in Study 2. Neuroticism may contribute to the strength of challenging experiences in uncontrolled settings.



An online survey of tobacco smoking cessation associated with naturalistic psychedelic use [119]

Journal Of Psychopharmacology • July 2017

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Data suggest psychedelics such as psilocybin and lysergic acid diethylamide (LSD) may hold therapeutic potential in the treatment of addictions, including tobacco dependence. This retrospective cross-sectional anonymous online survey characterized 358 individuals (52 females) who reported having quit or reduced smoking after ingesting a psychedelic in a non-laboratory setting ≥1 year ago. On average, participants smoked 14 cigarettes/day for 8 years, and had five previous quit attempts before their psychedelic experience. Of the 358 participants, 38% reported continuous smoking cessation after psychedelic use (quitters). Among quitters, 74% reported >2 years' abstinence. Of the 358 participants, 28% reported a persisting reduction in smoking (reducers), from a mode of 300 cigarettes/month before, to a mode of 1 cigarette/month after the experience. Among reducers, 62% reported >2 years of reduced smoking. Finally, 34% of the 358 participants (relapsers) reported a temporary smoking reduction before returning to baseline smoking levels, with a mode time range to relapse of 3-6 months. Relapsers rated their psychedelic experience significantly lower in personal meaning and spiritual significance than both other groups. Participants across all groups reported less severe affective withdrawal symptoms (e.g. depression, craving) after psychedelic use compared with previous quit attempts, suggesting a potential mechanism of action for psychedelic-associated smoking cessation/reduction. Changes in life priorities/values were endorsed as the most important psychological factor associated with smoking cessation/reduction. Results suggest psychedelics may hold promise in treating tobacco addiction as potentially mediated by spiritual experience, changed priorities/values, and improved emotional regulation.

Research on hallucinogenic drugs used in Shaman religious activities

Zhonghua Yi Shi Za Zhi • July 2017
[Article in Chinese]

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The development of medicine experienced a long history, and the origin of medicine is not appeared overnight. Due to the lack of historical data, the question of the origin of medicine has not been agreed upon. As an ancient primitive religion, Shamanism retains the use of hallucinogenic drugs in its early religious activities rather well, providing a guidance for exploring the cognition on drugs in early human. Through the review of the hallucinogenic plants used by shaman religious activities in different countries and areas, it was found that hallucinogenic drugs can be classified into two categories: single and mixed, which came mainly from plants and fungi, and the origin of hallucinogenic drugs has a high fitting degree with Shaman location. The study result suggests that, based on the worldwide research literature on the application of such hallucinogens with local characteristics in the shamanistic religious activities, it is very likely that important clues can be found to understand the facts of discovery and application of natural drugs, thus providing a new approach for the studies on the origin of drugs.

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An abstract of the article is available in PubMed, which may also have a link to the full text at the journal site
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Message ID: 851750617 (ipmc21)
Time: 2017/10/02 17:34:17

Locomotor and discriminative stimulus effects of four novel hallucinogens in rodents [809]

Behavioural Pharmacology • August 2017

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There has been increasing use of novel synthetic hallucinogenic compounds, 2-(4-bromo-2,5-dimethoxyphenyl)-N-(2-methoxybenzyl)ethanamine hydrochloride (25B-NBOMe), 2-(4-chloro-2,5-dimethoxyphenyl)-N-(2-methoxybenzyl)ethanamine hydrochloride (25C-NBOMe), 2-(4-iodo-2,5-dimethoxyphenyl)-N-(2-methoxybenzyl)ethanamine hydrochloride (25I-NBOMe), and N,N-diallyl-5-methoxy tryptamine (5-MeO-DALT), which have been associated with severe toxicities. These four compounds were tested for discriminative stimulus effects similar to a prototypical hallucinogen (–)-2,5-dimethoxy-4-methylamphetamine (DOM) and the entactogen (±)-3,4-methylenedioxymethamphetamine (MDMA). Locomotor activity in mice was tested to obtain dose range and time-course information. 25B-NBOMe, 25C-NBOMe, and 25I-NBOMe decreased locomotor activity. 5-MeO-DALT dose dependently increased locomotor activity, with a peak at 10 mg/kg. A higher dose (25 mg/kg) suppressed activity. 25B-NBOMe fully substituted (≥80%) in both DOM-trained and MDMA-trained rats at 0.5 mg/kg. However, higher doses produced much lower levels of drug-appropriate responding in both DOM-trained and MDMA-trained rats. 25C-NBOMe fully substituted in DOM-trained rats, but produced only 67% drug-appropriate responding in MDMA-trained rats at doses that suppressed responding. 25I-NBOMe produced 74–78% drug-appropriate responding in DOM-trained and MDMAtrained rats at doses that suppressed responding. 5-MeODALT fully substituted for DOM, but produced few or no MDMA-like effects. All of the compounds, except 25INBOMe, fully substituted for DOM, whereas only 25BNBOMe fully substituted for MDMA. However, the failure of 25I-NBOMe to fully substitute for either MDMA or DOM was more likely because of its substantial rate-depressant effects than weak discriminative stimulus effects. All of the compounds are likely to attract recreational users for their hallucinogenic properties, but probably of much less interest as substitutes for MDMA. Although no acute adverse effects were observed at the doses tested, the substantial toxicities reported in humans, coupled with the high likelihood for illicit use, suggests that these compounds have the same potential for abuse as other, currently scheduled compounds.

Novel Psychoactive Substances—Recent Progress on Neuropharmacological Mechanisms of Action for Selected Drugs [232]

Frontiers In Psychiatry • August 2017

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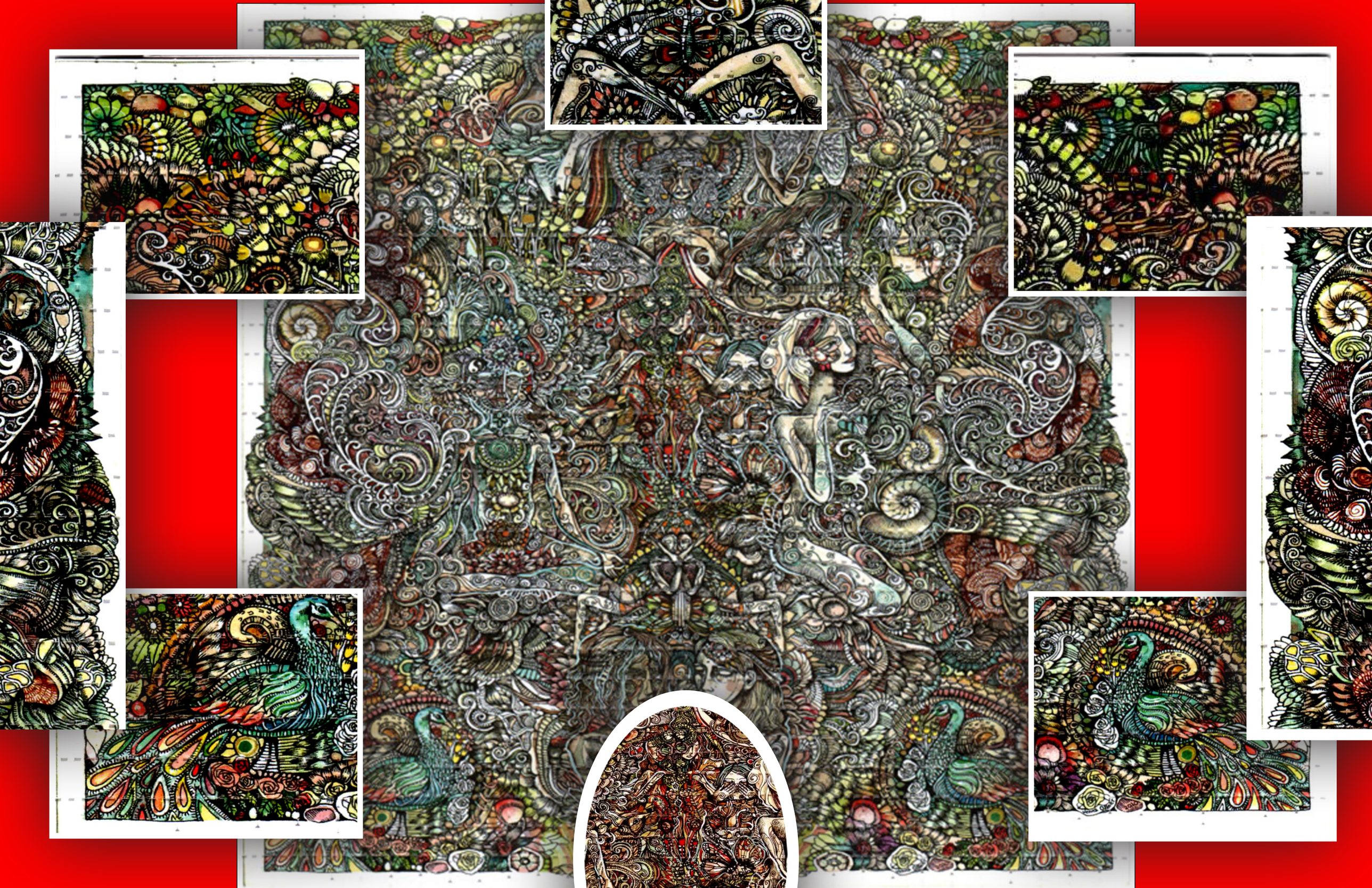
A feature of human culture is that we can learn to consume chemical compounds, derived from natural plants or synthetic fabrication, for their psychoactive effects. These drugs change the mental state and/or the behavioral performance of an individual and can be instrumentalized for various purposes. After the emergence of a novel psychoactive substance (NPS) and a period of experimental consumption, personal and medical benefits and harm potential of the NPS can be estimated on evidence base. This may lead to a legal classification of the NPS, which may range from limited medical use, controlled availability up to a complete ban of the drug form publicly accepted use. With these measures, however, a drug does not disappear, but frequently continues to be used, which eventually allows an even better estimate of the drug's properties. Thus, only in rare cases, there is a final verdict that is no more questioned. Instead, the view on a drug can change from tolerable to harmful but may also involve the new establishment of a desired medical application to a previously harmful drug. Here, we provide a summary review on a number of NPS for which the neuropharmacological evaluation has made important progress in recent years. They include mitragynine ("Kratom"), synthetic cannabinoids (e.g., "Spice"), dimethyltryptamine and novel serotonergic hallucinogens, the cathinones mephedrone and methylone, ketamine and novel dissociative drugs, γ-hydroxybutyrate, γ-butyrolactone, and 1,4-butanediol. This review shows not only emerging harm potentials but also some potential medical applications.



Psychedelic Drugs in Biomedicine [312]

Trends In Pharmacology Science • September 2017

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Psychedelic drugs, such as lysergic acid diethylamide (LSD), mescaline, and psilocybin, exert profound effects on brain and behavior. After decades of difficulties in studying these compounds, psychedelics are again being tested as potential treatments for intractable biomedical disorders. Preclinical research of psychedelics complements human neuroimaging studies and pilot clinical trials, suggesting these compounds as promising treatments for addiction, depression, anxiety, and other conditions. However, many questions regarding the mechanisms of action, safety, and efficacy of psychedelics remain. Here, we summarize recent preclinical and clinical data in this field, discuss their pharmacological mechanisms of action, and outline critical areas for future studies of psychedelic drugs, with the goal of maximizing the potential benefits of translational psychedelic biomedicine to patients.

Assessing the Psychedelic "After-Glow" in Ayahuasca Users: Post-Acute Neurometabolic and Functional Connectivity Changes Are Associated with Enhanced Mindfulness Capacities [150]

International Journal Of Neuropsychopharmacology • September 2017

Sampedro F1, de la Fuente Revenga M1, Valle M1, Roberto N1, Domínguez-Clavé E1Elices M1, Luna LE1, Crippa JAS1, Hallak JEC1
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Ayahuasca is a plant tea containing the psychedelic 5-HT2A agonist N,N-dimethyltryptamine and harmala monoamine-oxidase inhibitors. Acute administration leads to neurophysiological modifications in brain regions of the default mode network, purportedly through a glutamatergic mechanism. Post-acutely, ayahuasca potentiates mindfulness capacities in volunteers and induces rapid and sustained antidepressant effects in treatment-resistant patients. However, the mechanisms underlying these fast and maintained effects are poorly understood. Here, we investigated in an open-label uncontrolled study in 16 healthy volunteers ayahuasca-induced post-acute neurometabolic and connectivity modifications and their association with mindfulness measures. Using 1H-magnetic resonance spectroscopy and functional connectivity, we compared baseline and post-acute neurometabolites and seed-to-voxel connectivity in the posterior and anterior cingulate cortex after a single ayahuasca dose. Magnetic resonance spectroscopy showed post-acute reductions in glutamate+glutamine, creatine, and N-acetylaspartate+N-acetylaspartylglutamate in the posterior cingulate cortex. Connectivity was increased between the posterior cingulate cortex and the anterior cingulate cortex, and between the anterior cingulate cortex and limbic structures in the right medial temporal lobe. Glutamate+glutamine reductions correlated with increases in the "nonjudging" subscale of the Five Facets Mindfulness Questionnaire. Increased anterior cingulate cortex-medial temporal lobe connectivity correlated with increased scores on the self-compassion questionnaire. Post-acute neural changes predicted sustained elevations in nonjudging 2 months later.

CONCLUSIONS

These results support the involvement of glutamate neurotransmission in the effects of psychedelics in humans. They further suggest that neurometabolic changes in the posterior cingulate cortex, a key region within the default mode network, and increased connectivity between the anterior cingulate cortex and medial temporal lobe structures involved in emotion and memory potentially underlie the post-acute psychological effects of ayahuasca.

Possible role of biochemiluminescent photons for lysergic acid diethylamide (LSD)-induced phosphenes and visual hallucinations [124]

Reviews In Neuroscience • January 2017

Kapócs G, Scholkmann F, Salari V,
Császár N, Szőke H, Bókkon I.

Today, there is an increased interest in research on lysergic acid diethylamide (LSD) because it may offer new opportunities in psychotherapy under controlled settings. The more we know about how a drug works in the brain, the more opportunities there will be to exploit it in medicine. Here, based on our previously published papers and investigations, we suggest that LSD-induced visual hallucinations/phosphenes may be due to the transient enhancement of bioluminescent photons in the early retinotopic visual system in blind as well as healthy people.

A Receptor on Acid [268]

Cell • January 2017

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Wacker et al. report the crystal structure of LSD in complex with one of its major targets in the brain, the 5-HT2B receptor, the first such structure for any psychedelic drug. The results shed light on the molecular mechanisms underlying its ability to induce hallucinations with greater duration and potency than closely related compounds.

Lysergic acid diethylamide (LSD), also known as "acid," is one of the most potent psychedelic drugs. At low-microgram dosages, LSD can cause hallucinations (alteration of perception, emotion, and cognition), or "trips," that last for up to 15 hr. Albert Hofmann first synthesized LSD in 1938, but its psychedelic effects were only discovered five years later, when he accidentally exposed himself to trace amounts, resulting in a "not-unpleasant" condition characterized by an "extremely stimulated imagination" along with an "uninterrupted stream of fantastic pictures." He later confirmed that LSD was the culprit by self-administering 250 mg, now considered a heavy dose, and experienced the world's first intentional acid trip in part while bicycling home from his lab (Hofmann, 1979). LSD gained popularity in early '60s for recreational use but later became regulated as a type I substance. Use of LSD resurged in the middle '90s in the United States when, according to the Monitoring the Future study, 8.8% of 12th grade students reported that they had used LSD at least once. The percentage has declined to 2% since 2002, presumably due to enhanced control over LSD precursors (Johnston et al., 2016).

LSD has come to attention more recently because it shows promise for treating alcohol abuse and depression and in alleviating the anxiety of patients suffering terminally ill diseases. Although the drug targets a broad spectrum of receptors in vivo, it is believed to exert its psychedelic effects primarily by binding to the 5-HT2A serotonin receptor (Titeler et al., 1988), a G-protein-coupled receptor. However, the molecular mechanisms underlying its potent psychedelic effect have remained elusive. In this issue of Cell, Wacker et al. (2017) now report the crystal structure of LSD in complex with the closely related 5-HT2B receptor. The study establishes that LSD induces unique conformational changes in the receptor that likely underlie its psychedelic activity and sheds light on the structural basis for the high potency of LSD and the long duration of its effects.

The Fabric of Meaning and Subjective Effects in LSD-Induced States Depend on Serotonin 2A Receptor Activation [127]

Currents In Biology • February 2017

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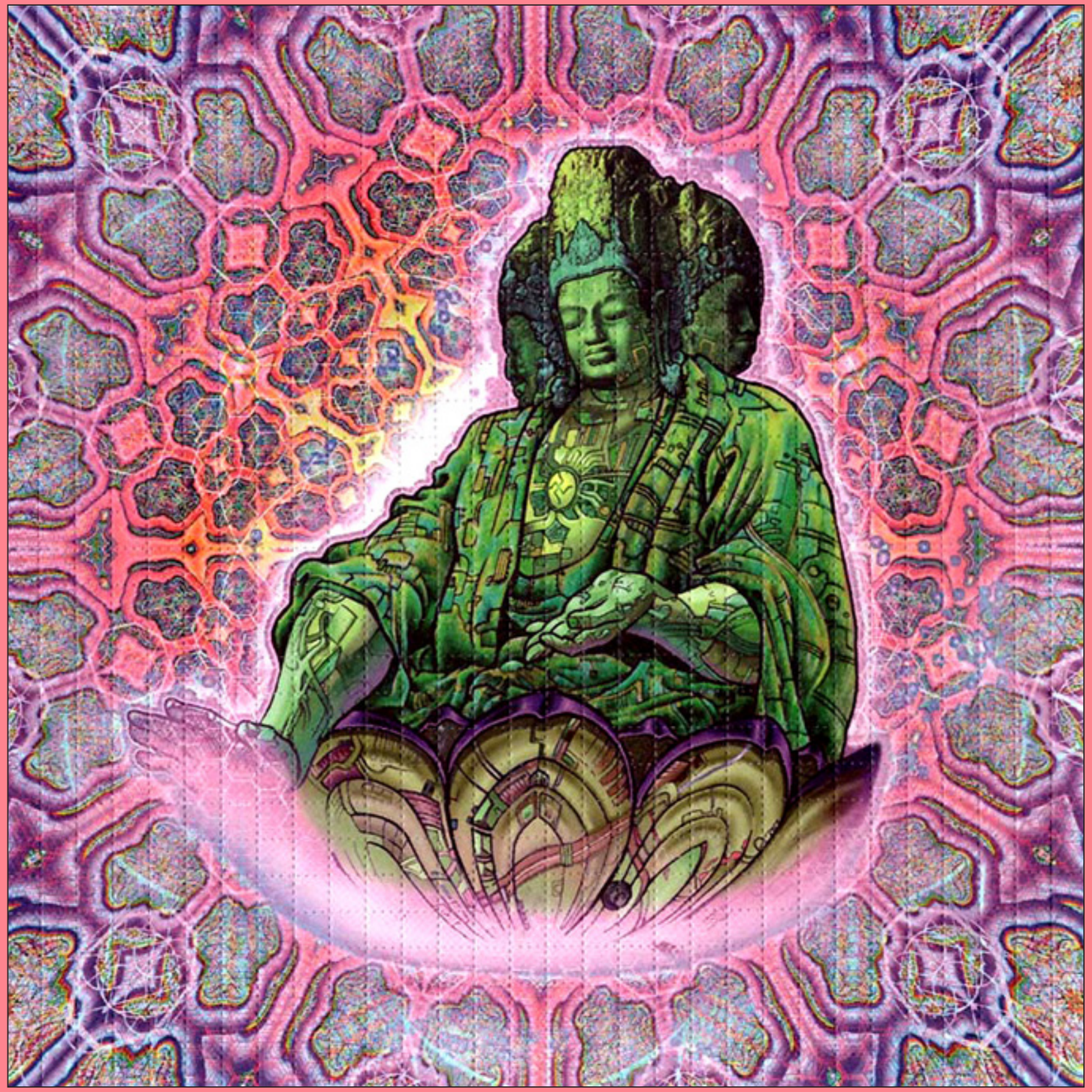
A core aspect of the human self is the attribution of personal relevance to everyday stimuli enabling us to experience our environment as meaningful [1]. However, abnormalities in the attribution of personal relevance to sensory experiences are also critical features of many psychiatric disorders [2, 3]. Despite their clinical relevance, the neurochemical and anatomical substrates enabling meaningful experiences are largely unknown. Therefore, we investigated the neuropharmacology of personal relevance processing in humans by combining fMRI and the administration of the mixed serotonin (5-HT) and dopamine receptor (R) agonist lysergic acid diethylamide (LSD), well known to alter the subjective meaning of percepts, with and without pretreatment with the 5-HT2AR antagonist ketanserin. General subjective LSD effects were fully blocked by ketanserin. In addition, ketanserin inhibited the LSD-induced attribution of personal relevance to previously meaningless stimuli and modulated the processing of meaningful stimuli in cortical midline structures. These findings point to the crucial role of the 5-HT2AR subtype and cortical midline regions in the generation and attribution of personal relevance. Our results thus increase our mechanistic understanding of personal relevance processing and reveal potential targets for the treatment of psychiatric illnesses characterized by alterations in personal relevance attribution.



Long-lasting subjective effects of LSD in normal subjects [173]

Psychopharmacology • September 2017

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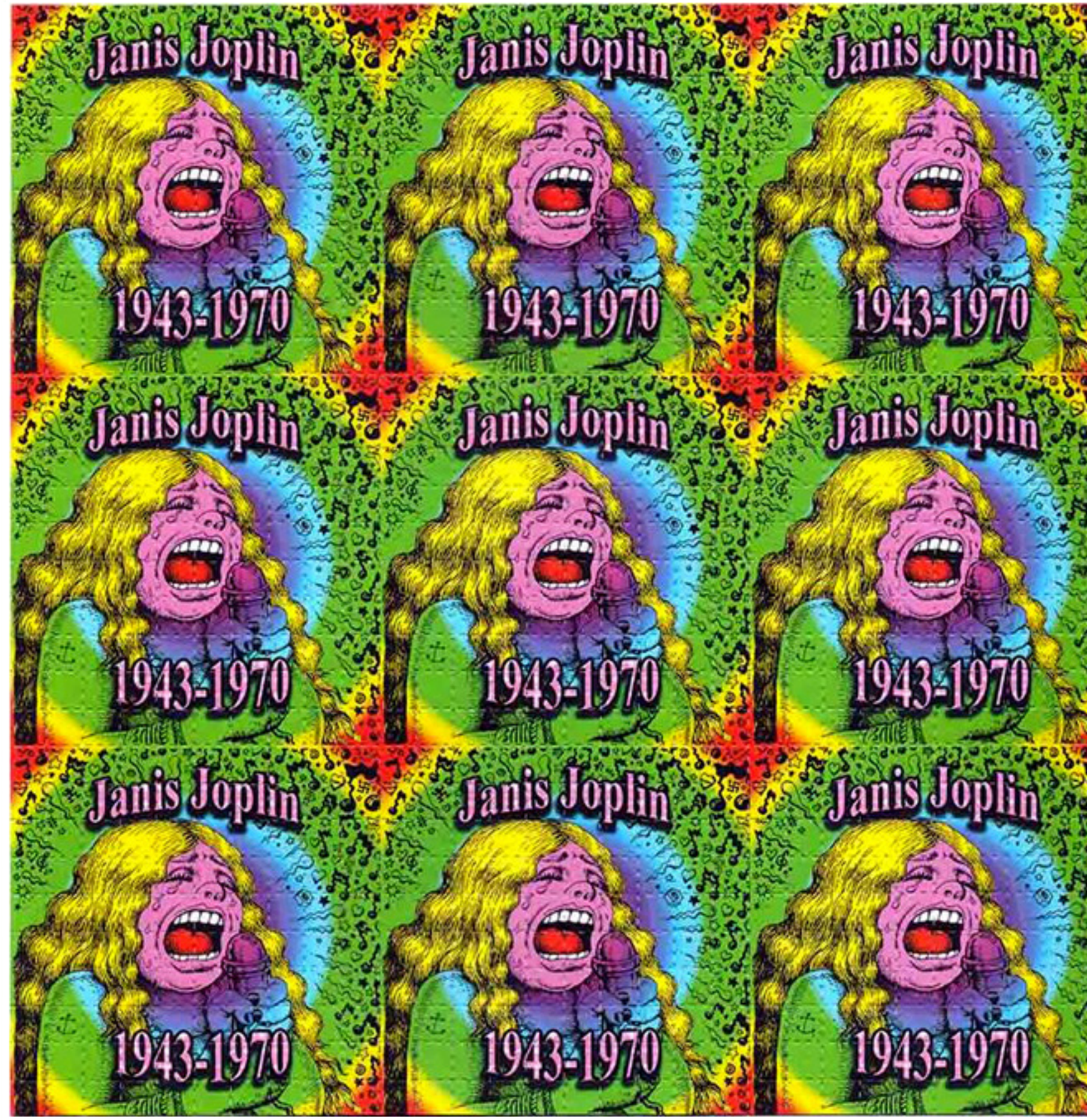
Lysergic acid diethylamide (LSD) and other serotonergic hallucinogens can induce profound alterations of consciousness and mystical-type experiences, with reportedly long-lasting effects on subjective well-being and personality. We investigated the lasting effects of a single dose of LSD (200 µg) that was administered in a laboratory setting in 16 healthy participants. The following outcome measures were assessed before and 1 and 12 months after LSD administration: Persisting Effects Questionnaire (PEQ), Mysticism Scale (MS), Death Transcendence Scale (DTS), NEO-Five Factor Inventory (NEO-FFI), and State-Trait Anxiety Inventory (STAI). On the PEQ, positive attitudes about life and/or self, positive mood changes, altruistic/positive social effects, positive behavioral changes, and well-being/life satisfaction significantly increased at 1 and 12 months and were subjectively attributed by the subjects to the LSD experience. Five-Dimensions of Altered States of Consciousness (5D-ASC) total scores, reflecting acutely induced alterations in consciousness, and Mystical Experience Questionnaire (MEQ30) total scores correlated with changes in well-being/life satisfaction 12 months after LSD administration. No changes in negative attitudes, negative mood, antisocial/negative social effects, or negative behavior were attributed to the LSD experience. After 12 months, 10 of 14 participants rated their LSD experience as among the top 10 most meaningful experiences in their lives. Five participants rated the LSD experience among the five most spiritually meaningful experiences in their lives. On the MS and DTS, ratings of mystical experiences significantly increased 1 and 12 months after LSD administration compared with the pre-LSD screening. No relevant changes in personality measures were found. In healthy research subjects, the administration of a single dose of LSD (200 µg) in a safe setting was subjectively considered a personally meaningful experience that had long-lasting subjective positive effects.

Trial Registration:
Registration identification number: NCT01878942



Effect of Hallucinogens on Unconditioned Behavior [128]

Current Topics In Behavioral Neuroscience
February 2017

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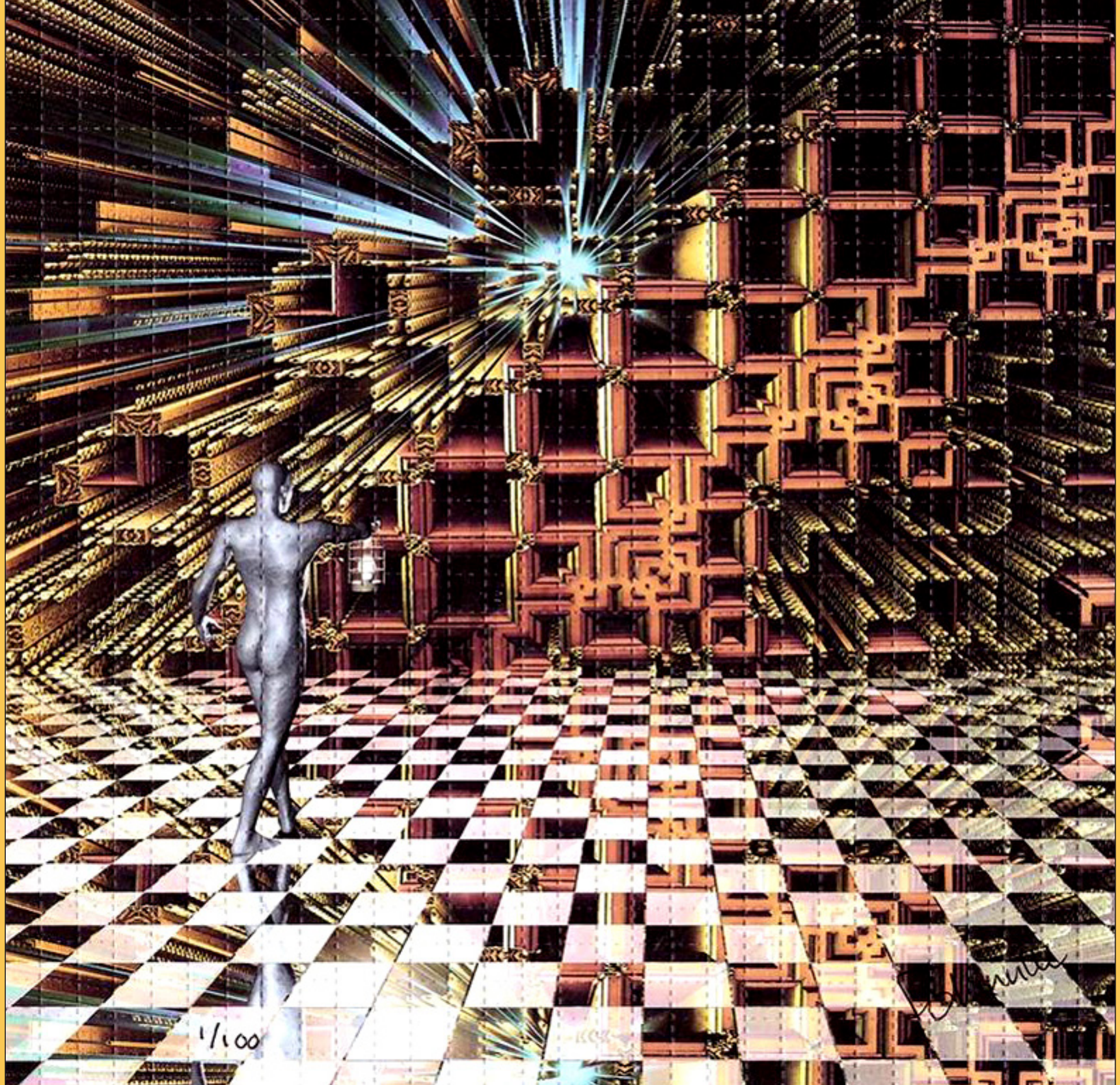
Because of the ethical and regulatory hurdles associated with human studies, much of what is known about the psychopharmacology of hallucinogens has been derived from animal models. However, developing reliable animal models has proven to be a challenging task due to the complexity and variability of hallucinogen effects in humans. This chapter focuses on three animal models that are frequently used to test the effects of hallucinogens on unconditioned behavior: head twitch response (HTR), prepulse inhibition of startle (PPI), and exploratory behavior. The HTR has demonstrated considerable utility in the neurochemical actions of hallucinogens. However, the latter two models have clearer conceptual bridges to human phenomenology. Consistent with the known mechanism of action of hallucinogens in humans, the behavioral effects of hallucinogens in rodents are mediated primarily by activation of 5-HT2A receptors. There is evidence, however, that other receptors may play secondary roles. The structure-activity relationships (SAR) of hallucinogens are reviewed in relation to each model, with a focus on the HTR in rats and mice.



Pharmacokinetics and Pharmacodynamics of Lysergic Acid Diethylamide in Healthy Subjects [129]

Clinical Pharmacokinetics • February 2017

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Lysergic acid diethylamide (LSD) is used recreationally and in clinical research. The aim of the present study was to characterize the pharmacokinetics and exposure-response relationship of oral LSD. We analyzed pharmacokinetic data from two published placebo-controlled, double-blind, cross-over studies using oral administration of LSD 100 and 200 µg in 24 and 16 subjects, respectively. The pharmacokinetics of the 100-µg dose is shown for the first time and data for the 200-µg dose were reanalyzed and included. Plasma concentrations of LSD, subjective effects, and vital signs were repeatedly assessed. Pharmacokinetic parameters were determined using compartmental modeling. Concentration-effect relationships were described using pharmacokinetic-pharmacodynamic modeling. Geometric mean (95% confidence interval) maximum plasma concentration values of 1.3 (1.2-1.9) and 3.1 (2.6-4.0) ng/mL were reached 1.4 and 1.5 h after administration of 100 and 200 µg LSD, respectively. The plasma half-life was 2.6 h (2.2-3.4 h). The subjective effects lasted (mean ± standard deviation) 8.2 ± 2.1 and 11.6 ± 1.7 h for the 100- and 200-µg LSD doses, respectively. Subjective peak effects were reached 2.8 and 2.5 h after administration of LSD 100 and 200 µg, respectively. A close relationship was observed between the LSD concentration and subjective response within subjects, with moderate counterclockwise hysteresis. Half-maximal effective concentration values were in the range of 1 ng/mL. No correlations were found between plasma LSD concentrations and the effects of LSD across subjects at or near maximum plasma concentration and within dose groups. The present pharmacokinetic data are important for the evaluation of clinical study findings (e.g., functional magnetic resonance imaging studies) and the interpretation of LSD intoxication. Oral LSD presented dose-proportional pharmacokinetics and first-order elimination up to 12 h. The effects of LSD were related to changes in plasma concentrations over time, with no evidence of acute tolerance.

Trial Registration: NCT02308969, NCT01878942

Return of the lysergamides Part I: Analytical and behavioural characterization of 1-propionyl-d-lysergic acid diethylamide (1P-LSD) [278]

Drug Testing & Analysis • September 2016 [Parts 2, 3 and 4 follow]

Brandt SD1, Kavanagh PV2, Westphal F3, Stratford A4
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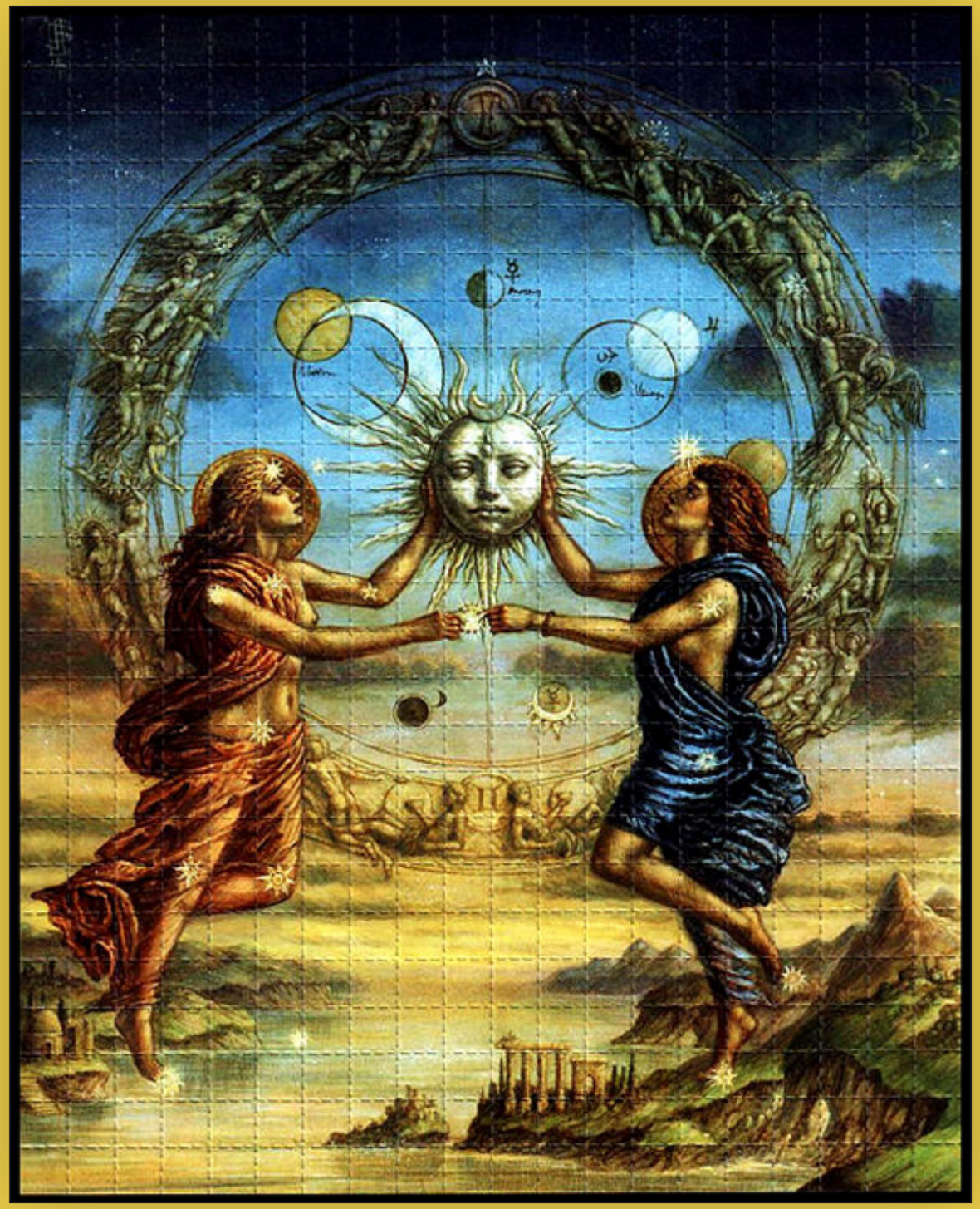
1-Propionyl-d-lysergic acid diethylamide hemitartrate (1P-LSD) has become available as a 'research chemical' in the form of blotters and powdered material. This non-controlled derivative of d-lysergic acid diethylamide (LSD) has previously not been described in the published literature despite being closely related to 1-acetyl-LSD (ALD-52), which was developed in the 1950s. This study describes the characterization of 1P-LSD in comparison with LSD using various chromatographic and mass spectrometric methods, infrared and nuclear magnetic resonance spectroscopy. An important feature common to LSD and other serotonergic hallucinogens is that they produce 5-HT2A -receptor activation and induce the head-twitch response (HTR) in rats and mice. In order to assess whether 1P-LSD displays LSD-like properties and activates the 5-HT2A receptor, male C57BL/6 J mice were injected with vehicle (saline) or 1P-LSD (0.025-0.8 mg/kg, IP) and HTR assessed for 30 min using magnetometer coil recordings. It was found that 1P-LSD produced a dose-dependent increase in HTR counts, and that it had ~38% (ED50 = 349.6 nmol/kg) of the potency of LSD (ED50 = 132.8 nmol/kg). Furthermore, HTR was abolished when 1P-LSD administration followed pretreatment with the selective 5-HT2A receptor antagonist M100907 (0.1 mg/kg, SC), which was consistent with the concept that the behavioural response was mediated by activation of the 5-HT2A receptor. These results indicate that 1P-LSD produces LSD-like effects in mice, consistent with its classification as a serotonergic hallucinogen. Nevertheless, the extent to which 1P-LSD might show psychoactive effects in humans similar to LSD remains to be investigated.



Return of the lysergamides Part II: Analytical and behavioural characterization of N6-allyl-6-norlysergic acid diethylamide (AL-LAD) and (2'S,4'S)-lysergic acid 2,4-dimethylazetidide (LSZ) [62]

Drug Testing & Analysis • January 2017

Brandt SD1, Kavanagh PV2, Westphal F3, Elliott SP4, Wallach J5
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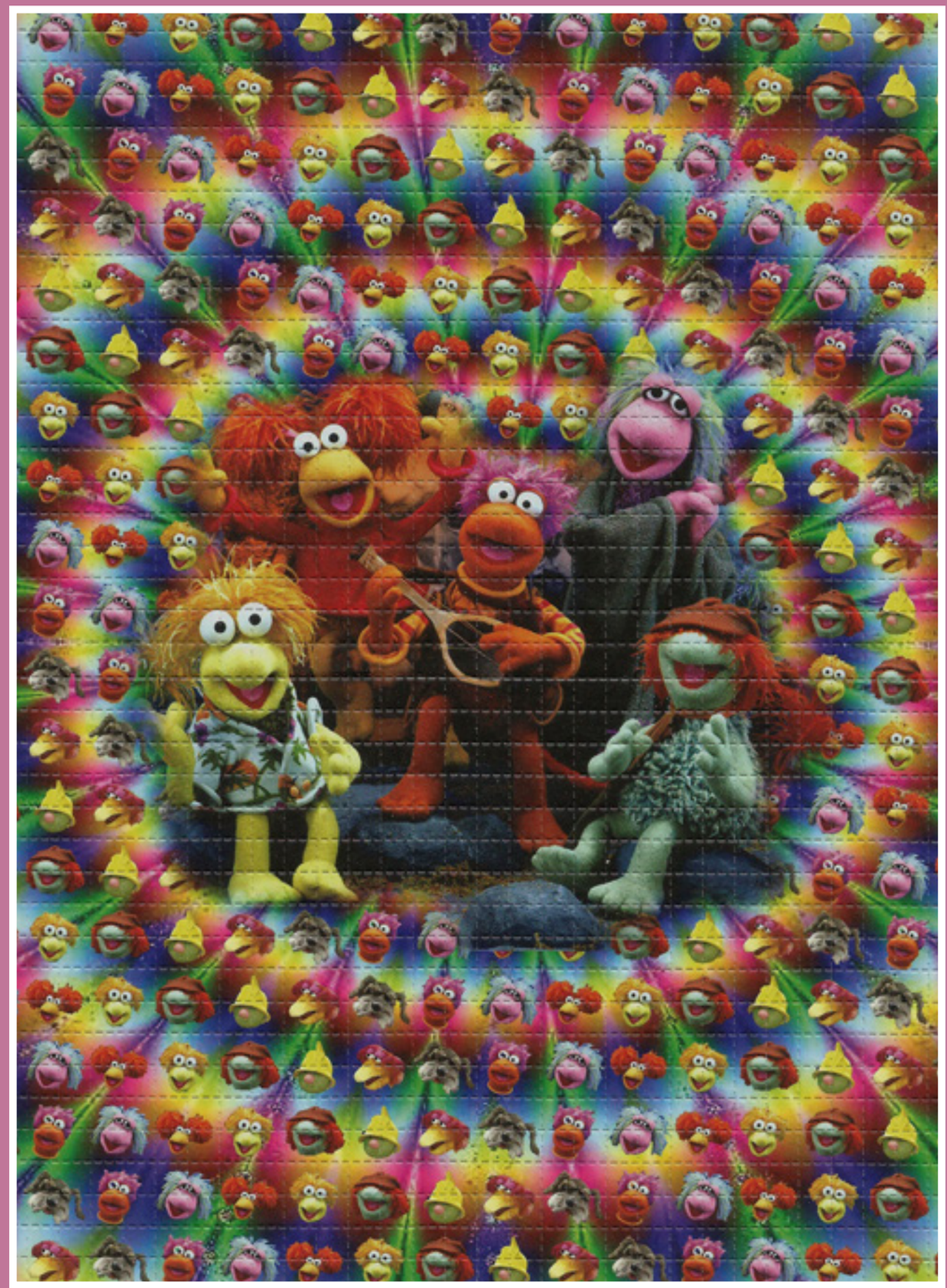
Lysergic acid N,N-diethylamide (LSD) is perhaps one of the most intriguing psychoactive substances known and numerous analogs have been explored to varying extents in previous decades. In 2013, N6 -allyl-6-norlysergic acid diethylamide (AL-LAD) and (2'S,4'S)-lysergic acid 2,4-dimethylazetidide (LSZ) appeared on the 'research chemicals'/new psychoactive substances (NPS) market in both powdered and blotter form. This study reports the analytical characterization of powdered AL-LAD and LSZ tartrate samples and their semi-quantitative determination on blotter paper. Included in this study was the use of nuclear magnetic resonance (NMR) spectroscopy, gas chromatography-mass spectrometry (GC-MS), low and high mass accuracy electrospray MS(/MS), high performance liquid chromatography diode array detection and GC solid-state infrared analysis. One feature shared by serotonergic psychedelics, such as LSD, is the ability to mediate behavioural responses via activation of 5-HT2A receptors. Both AL-LAD and LSZ displayed LSD-like responses in male C57BL/6 J mice when employing the head-twitch response (HTR) assay. AL-LAD and LSZ produced nearly identical inverted-U-shaped dose-dependent effects, with the maximal responses occurring at 200 µg/kg. Analysis of the dose responses by nonlinear regression confirmed that LSZ (ED50 = 114.2 nmol/kg) was equipotent to LSD (ED50 = 132.8 nmol/kg) in mice, whereas AL-LAD was slightly less potent (ED50 = 174.9 nmol/kg). The extent to which a comparison in potency can be translated directly to humans requires further investigation. Chemical and pharmacological data obtained from NPS may assist research communities that are interested in various aspects related to substance use and forensic identification.



Return of the lysergamides Part III: Analytical characterization of N6-ethyl-6-norlysergic acid diethylamide (ETH-LAD) and 1-propionyl ETH-LAD (1P-ETH-LAD) [63]

Drug Testing & Analysis • March 2017

Brandt SD1, Kavanagh PV2, Westphal F3, Elliott SP4
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The psychoactive properties of lysergic acid diethylamide (LSD) have fascinated scientists across disciplines and the exploration of other analogues and derivatives has been motivated by deepening the understanding of ligand-receptor interactions at the molecular level as well as by the search for new therapeutics. Several LSD congeners have appeared on the new psychoactive substances (NPS) market in the form of blotters or powders. Examples include 1-propionyl-LSD (1P-LSD), AL-LAD, and LSZ. The absence of analytical data for novel compounds is a frequent challenge encountered in clinical and toxicological investigations. Two newly emerging lysergamides, namely N6 -ethyl-6-norlysergic acid diethylamide (ETH-LAD) and 1P-ETH-LAD, were characterized by gas chromatography-mass spectrometry (GC-MS), low and high mass accuracy electrospray MS(/MS), GC solid-state infrared analysis, high performance liquid chromatography diode array detection as well as nuclear magnetic resonance spectroscopy. Limited analytical data for ETH-LAD were previously available, whereas information about 1P-ETH-LAD has not previously been encountered in the scientific literature. This study extends the characterization of lysergamides distributed on the NPS market, which will help to make analytical data available to clinicians, toxicologists, and other stakeholders who are likely to encounter these substances. The analysis of a test incubation of 1P-ETH-LAD with human serum at 37°C by LC single quadrupole MS at various time points (0-6 h, once per hour and one measurement after 24 h) revealed the formation of ETH-LAD, suggesting that 1P-ETH-LAD might serve as a pro-drug. 1P-ETH-LAD was still detectable in serum after 24 hours.

Return of the lysergamides Part IV: Analytical and pharmacological characterization of lysergic acid morpholide (LSM-775) [64]

Drug Testing & Analysis • March 2017

Brandt SD1, Kavanagh PV2, Twamley B3, Westphal F4, Elliott SP5, Wallach J6, Stratford A7, Klein LM8, McCorvy JD9, Nichols DE10, Halberstadt AL11

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Lysergic acid diethylamide (LSD) is perhaps one of the best-known psychoactive substances and many structural modifications of this prototypical lysergamide have been investigated. Several lysergamides were recently encountered as 'research chemicals' or new psychoactive substances (NPS). Although lysergic acid morpholide (LSM-775) appeared on the NPS market in 2013, there is disagreement in the literature regarding the potency and psychoactive properties of LSM-775 in humans. The present investigation attempts to address the gap of information that exists regarding the analytical profile and pharmacological effects of LSM-775. A powdered sample of LSM-775 was characterized by X-ray crystallography, nuclear magnetic resonance spectroscopy (NMR), gas chromatography mass spectrometry (GC-MS), high mass accuracy electrospray MS/MS, high performance liquid chromatography (HPLC) diode array detection, HPLC quadrupole MS, and GC solid-state infrared analysis. Screening for receptor affinity and functional efficacy revealed that LSM-775 acts as a nonselective agonist at 5-HT1A and 5-HT2A receptors. Head twitch studies were conducted in C57BL/6J mice to determine whether LSM-775 activates 5-HT2A receptors and produces hallucinogen-like effects in vivo. LSM-775 did not induce the head twitch response unless 5-HT1A receptors were blocked by pretreatment with the antagonist WAY-100,635 (1 mg/kg, subcutaneous). These findings suggest that 5-HT1A activation by LSM-775 masks its ability to induce the head twitch response, which is potentially consistent with reports in the literature indicating that LSM-775 is only capable of producing weak LSD-like effects in humans.

Disrupted integration of sensory stimuli with information about the movement of the body as a mechanism explaining LSD-induced experience

Med Hypotheses • March 2017

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LSD (lysergic acid diethylamide) is a model psychedelic drug used to study mechanism underlying the effects induced by hallucinogens. However, despite advanced knowledge about molecular mechanism responsible for the effects induced by LSD and other related substances acting at serotonergic 5-HT2a receptors, we still do not understand how these drugs trigger specific sensory experiences. LSD-induced experience is characterised by perception of movement in the environment and by presence of various bodily sensations such as floating in space, merging into surroundings and movement out of the physical body (the out-of-body experience). It means that a large part of the experience induced by the LSD can be simplified to the illusory movement that can be attributed to the self or to external objects. The phenomenology of the LSD-induced experience has been combined with the fact that serotonergic neurons provide all major parts of the brain with information about the level of tonic motor activity, occurrence of external stimuli and the execution of orienting responses. Therefore, it has been proposed that LSD-induced stimulation of 5-HT2a receptors disrupts the integration of the sensory stimuli with information about the movement of the body leading to perception of illusory movement.

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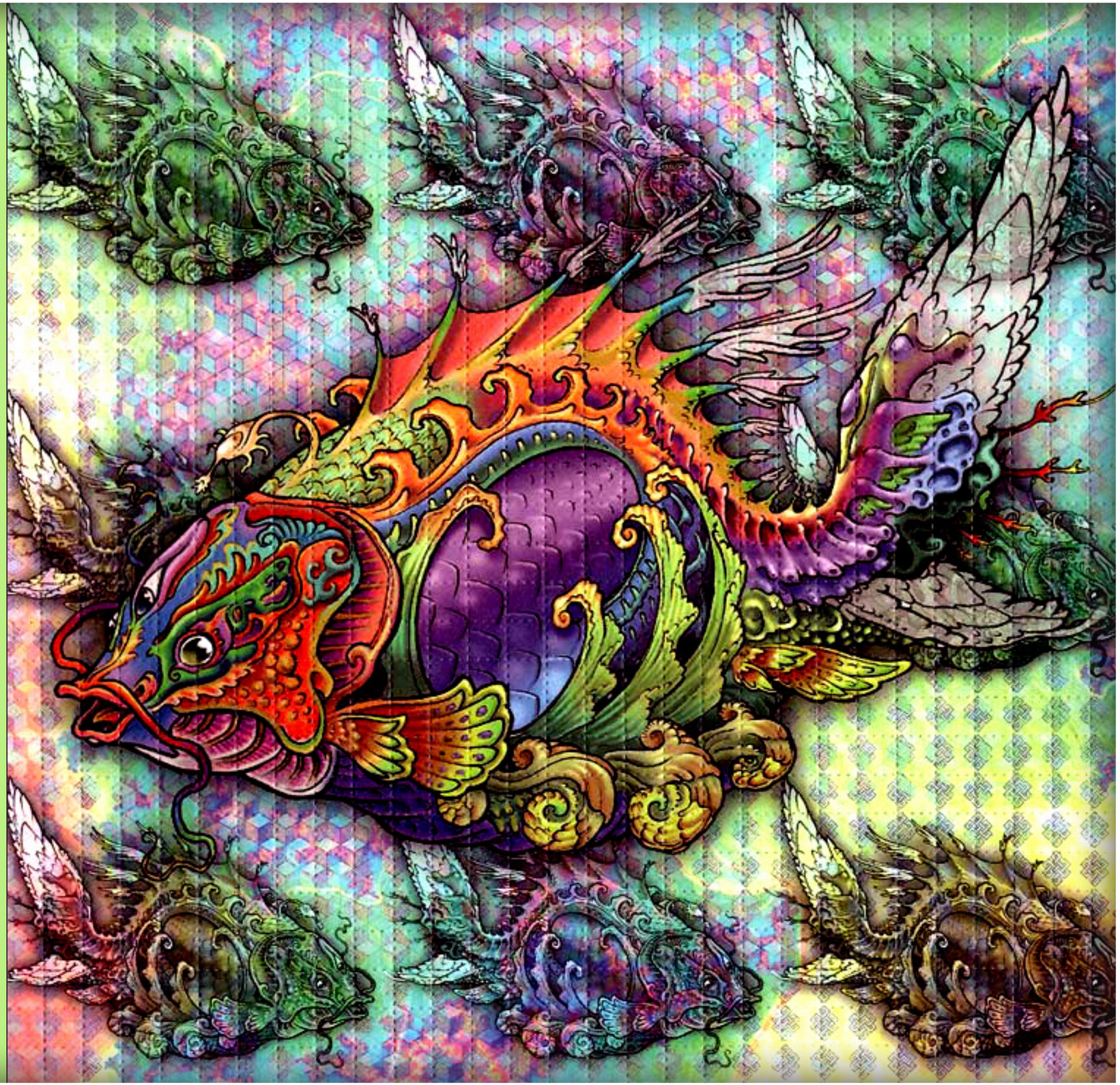

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